Notice of Allowability	Application No.	Applicant(s)	
	10/780,399	RAO ET AL.	
	Examiner	Art Unit	
	GAILENE R. GABEL	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *Applicant's Amdt. filed 1/10/10 and Interview Summary on 4/7/10*.

2. ☒ The allowed claim(s) is/are *claims 44-46, 48-55, and 57-61; now renumbered as claims 1-16, respectively*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *4/7/10* .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/GAILENE R. GABEL/ Primary Examiner, Art Unit 1641	4/7/10

EXAMINER'S AMENDMENT

1. An extension of time under 37 CFR 1.136(a) is required in order to make an examiner's amendment which places this application in condition for allowance. During a telephone conversation conducted April 7, 2010, Mr. Joseph Aceto requested an extension of time for 1 MONTH(S) and authorized the Director to charge Deposit Account No. 10-0750 the required fee for this extension and authorized the following examiner's amendment. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. The application has been amended as follows:

In claim 44, step a), line 1 after "obtaining a", "biological specimen" has been deleted and --blood sample-- has been inserted therefor; then after "from a test subject, said", "specimen" has been deleted and --sample-- has been inserted therefor.

In claim 44, step a), line 2 after "intact malignant", --cancer-- has been inserted; and then after "cells", --of epithelial cell origin-- has been inserted.

In claim 44, step a), part i), after "cell fragments derived from", --said-- has been inserted; and then after "malignant cells,", "or" has been deleted and --and/or-- has been inserted therefor.

In claim 44, step a), part ii), after “cellular debris derived from”, --said-- has been inserted.

In claim 44, step b), line 1 after “said intact malignant cells”, --said-- has been inserted.

In claim 44, step b), line 2 after “cellular debris wherein said”, “biological” has been deleted and --blood-- has been inserted, therefor.

In claim 44, step b), line 4-5 after “a first biospecific ligand which reacts”, --and binds-- has been inserted; then after “specifically”, “with” has been deleted and --to an epitope present in each of-- has been inserted therefor; then after “said intact malignant cells,”, “and” has been deleted; and after “said cell fragments”, “or” has been deleted and --and-- has been inserted therefor; and then after “said cellular debris to form”, “a” has been deleted.

In claim 44, step b), line 6 after “specific binding,”, “complex” has been deleted and --complexes-- has been inserted therefor.

In claim 44, step c), line 1 after “specific binding,”, “complex” has been deleted and --complexes formed in step b)-- has been inserted therefor.

In claim 44, step d), line 2 after “specific binding,”, “complex” has been deleted and --complexes in step c)--.

In claim 44, step d), line 4 after “malignant cells,”, “and” has been deleted; and then after “said cell fragments”, “or” has been deleted and --and-- has been inserted therefor.

In claim 44, step d), line 5 after “exclusion of other specimen components”, --wherein the receptor is present in malignant tumor cells of epithelial cell origin-- has been inserted.

In claim 44, step e), line 1, before “analyzing,”, --differentially-- has been inserted; and then after “labeled malignant cells,”, “and” has been deleted.

In claim 44, step e), line 2 after “fragments”, “or” has been deleted and --and-- has been inserted therefor; and then after “said labeled cellular debris”, --in step d)-- has been inserted.

Claim 44 should therefore recite:

Claim 44. A method for monitoring malignancy in a test subject comprising:

a. obtaining a blood sample from a test subject, said sample comprising a mixed cell population suspected of containing intact malignant cancer cells of epithelial cell origin and further comprising:

i. cell fragments derived from said malignant cells, and/or

ii. cellular debris derived from said malignant cells;

b. preparing a sample with magnetically-labeled said intact malignant cells, said cell fragments and said cellular debris wherein said blood sample is mixed with colloidal magnetic particles, having a size range between 90 to 150 nm and a bovine serum albumin coating using high temperature, coupled to a first biospecific ligand which reacts and binds specifically to an epitope present in each of said intact malignant cells, said cell fragments and said cellular debris to form specific binding complexes with said colloidal magnetic particles and first biospecific ligand;

c. exposing said specific binding complexes formed in step b) to an externally- applied high gradient magnetic field to the substantial exclusion of other specimen components;

d. contacting said specific binding complexes in step c) with at least one additional biospecific ligand forming a specific binding pair with a receptor of said intact malignant cells, said cell fragments and

said cellular debris, to the substantial exclusion of other specimen components, wherein the receptor is present in malignant tumor cells of epithelial cell origin;

e. differentially analyzing amounts of said labeled malignant cells, said labeled cell fragments and said labeled cellular debris in step d) over time, a change in the numerical proportions of said labeled malignant cells, said labeled cell fragments, and said labeled cellular debris indicating a change of malignancy.

In claim 45, after “wherein said”, “biological specimen” has been deleted; and then after “blood”, --sample is whole blood sample-- has been inserted.

In claim 46, line 1 after “wherein after said”, “biological specimen” has been deleted and --blood sample is-- has been inserted therefor.

In claim 46, line 2 after “an agent capable of stabilizing said”, “biological specimen” has been deleted and --blood sample-- has been inserted therefor.

In claim 48, lines 3-4, after “said intact malignant cells,”, “and” has been deleted; then after “said cell fragments”, “or” has been deleted and --and-- has been inserted therefor.

In claim 50, line 3 after “wherein said additional biospecific ligand is”, --directed against-- has been inserted.

In claim 51, line 3 after “and wherein said additional biospecific ligand is”, --directed against-- has been inserted.

In claim 53, step a), line 1 after “obtaining a”, “biological specimen” has been deleted and --blood sample-- has been inserted therefor; and then after “from a test subject, said”, “specimen” has been deleted and --sample-- has been inserted therefor.

In claim 53, step a), line 2 after “intact malignant”, --cancer-- has been inserted; then after “cells”, --of epithelial cell origin-- has been inserted; and then after “and clusters of”, --said-- has been inserted.

In claim 53, step b), line 2 after “malignant cells wherein said”, “biological” has been deleted and --blood-- has been inserted therefor.

In claim 53, step b), lines 4-5 after “a first biospecific ligand which reacts”, --and binds-- has been inserted and then after “specifically”, “with” has been deleted and --to an epitope present in each of-- has been inserted therefor; and then after “said clusters of malignant cells to form”, “a” has been deleted.

In claim 53, step b), line 6 after “binding,”, “complex” has been deleted and --complexes-- has been inserted therefor.

In claim 53, step c), line 1 after “specific binding,”, “complex” has been deleted and --complexes formed in step b)-- has been inserted.

In claim 53, step d), line 2 after “specific binding,”, “complex” has been deleted and --complexes in step c)-- has been inserted therefor.

In claim 53, step d), lines 4-5 after “to the exclusion of other specimen components”, --wherein the receptor is present in malignant tumor cells of epithelial cell origin-- has been inserted.

In claim 53, step e), line 1 before “analyzing,”, --differentially-- has been inserted.

In claim 53, step e), line 2 after “malignant cells,” --in step d)-- has been inserted.

Claim 53 should therefore recite:

Claim 53. A method for monitoring malignancy in a test subject comprising:

a. obtaining a blood sample from a test subject, said sample comprising a mixed cell population suspected of containing intact malignant cancer cells of epithelial cell origin and clusters of said malignant cells;

b. preparing a sample with magnetically-labeled said intact malignant cells and said clusters of malignant cells wherein said blood sample is mixed with colloidal magnetic particles, having a size range between 90 to 150 nm and a bovine serum albumin coating using high temperature, coupled to a first biospecific ligand which reacts and binds specifically to an epitope present in each of said intact malignant cells and said clusters of malignant cells to form specific binding complexes with said colloidal magnetic particles and first biospecific ligand;

c. exposing said specific binding complexes formed in step b) to an externally- applied high gradient magnetic field to the substantial exclusion of other specimen components;

d. contacting said specific binding complexes in step c) with at least one additional biospecific ligand forming a specific binding pair with a receptor of said intact malignant cells and said clusters of malignant cells, to the substantial exclusion of other specimen components, wherein the receptor is present in malignant tumor cells of epithelial cell origin;

e. differentially analyzing amounts of said labeled malignant cells and said labeled clusters of malignant cells in step d) over time, a change in the numerical proportions of said labeled malignant cells and said labeled clusters of malignant cells indicating a change of malignancy.

In claim 54, after “wherein said”, “biological specimen” has been deleted; and then after “blood”, --sample is whole blood sample-- has been inserted.

In claim 55, line 1 after “wherein after said”, “biological specimen” has been deleted and --blood sample is-- has been inserted therefor.

In claim 55, line 2 after “an agent capable of stabilizing said”, “biological specimen” has been deleted and --blood sample-- has been inserted therefor.

In claim 59, preamble after “A kit for assaying a”, “biological specimen” has been deleted and --blood sample suspected of containing intact malignant cancer cells of epithelial cell origin-- has been inserted therefor; then after “the presence of malignant cells,”, “and” has been deleted; and then after “cell fragments derived from malignant cells”, “or” has been deleted and --and-- has been inserted therefor.

In claim 59, part a), subpart ii), after “a protein base coating”, “material” has been deleted and --comprising bovine serum albumin-- has been inserted therefor.

In claim 59, part a), subpart iii), line 1, after "an antibody that binds specifically to”, “a first characteristic determinant” has been deleted and --an epitope present in each-- has been inserted therefor;

In claim 59, part a), subpart iii), line 2 after “malignant cell, “and" has been deleted; then after “said cell fragments”, “or” has been deleted and --and-- has been inserted therefor.

In claim 59, part a), subpart iii), line 3 after “coupled to said”, --protein-- has been inserted; and then after “base coating”, “material” has been deleted and --on the colloidal magnetic nanoparticle-- has been inserted therefor.

In claim 59, part b), line 1 after “at least one antibody having binding specificity for a”, “second characteristic determinant” has been deleted and --receptor-- has been inserted therefor.

In claim 59, part b), line 2 after “said malignant cell,”, “and” has been deleted; then after “said cell fragments”, “or” has been deleted and --and-- has been inserted therefor; and then after “said cellular debris”, --,and wherein the receptor is present in malignant tumor cells of epithelial cell origin-- has been inserted.

In claim 59, part c) after “an agent capable of staining further”, --morphological-- has been inserted; then after “said malignant cells,”, “and” has been deleted; then after “said cell fragments”, “or” has been deleted and --and-- has been inserted therefor.

Claim 59 should therefor recite:

Claim 59. A kit for assaying a blood sample suspected of containing intact malignant cancer cells of epithelial cell origin for the presence of malignant cells, cell fragments derived from malignant cells and cellular debris derived from malignant cells, comprising:

a. coated colloidal magnetic nanoparticles comprising:

i. a magnetic core material having a size range between 90 to 150 nm;

ii. a protein base coating comprising bovine serum albumin applied using high temperature; and

iii. an antibody that binds specifically to an epitope present in each of said intact malignant cells, said cell fragments and said cellular debris, wherein said antibody is coupled to said protein base coating on the colloidal magnetic nanoparticle;

b. at least one antibody having binding specificity for a receptor of said malignant cell, said cell fragments and said cellular debris, and wherein the receptor is present in malignant tumor cells of epithelial cell origin; and

c. an agent capable of staining further morphological features of said malignant cells, said cell fragments and said cellular debris.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GAILENE R. GABEL whose telephone number is (571)272-0820. The examiner can normally be reached on Monday, Tuesday, Thursday, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GAILENE R. GABEL/

Primary Examiner, Art Unit 1641

April 7, 2010